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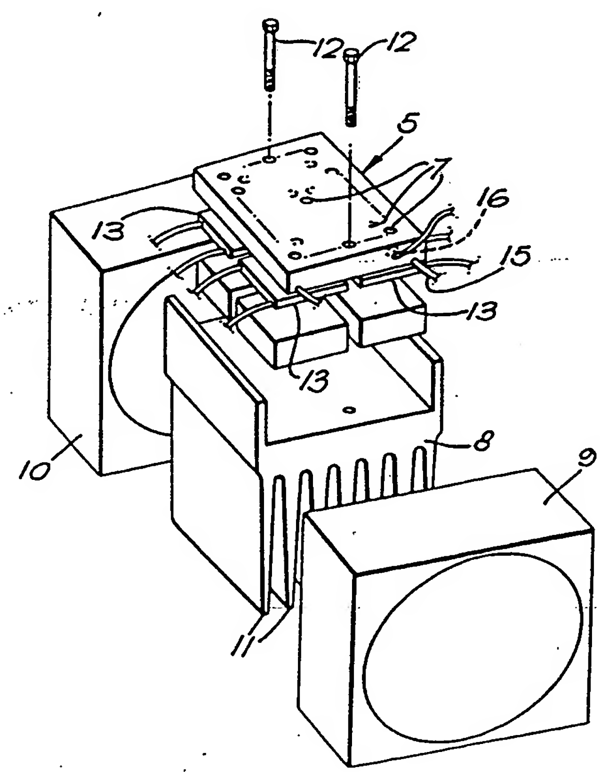

(57) Abstract

A biochemical incubator has a reaction plate (5) directly heated by a resistive heater (15) and cooled by Peltier devices (13), a heat sink (8) and fans (9, 10).

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Biochemical Reaction Machine

Background of the Invention

The present invention relates to a biochemical reaction machine.

Biochemical reaction machines exist for heating and cooling reagents in accordance with a temperature/time programme memorizede by a computer. Such a machine in combination with a computer is described in EP-A2-203,069. This machine comprises a reaction plate for transferring heat to and from reagents accommodated by the reaction plate; means for cooling the reaction plate, including a solid state heat pump in thermal contact on one side with the reaction plate and a heat sink in thermal contact with the other side of the solid state heat pump; and means for heating the reaction plate.

The Invention

The object of the present invention is to provide an improved biochemical reaction machine.

In a biochemical reaction machine of the invention the heating means is adapted and arranged to transfer heat direct to the reaction plate substantially independently of heat transfer from the heat sink by the heat pump.

Conveniently the solid state heat pump comprises a plurality of Peltier effect devices.

Preferably the heating means is an ohmic heating element incorporated with the reaction plate.

Whilst the ohmic heating element may be accommodated in bores in the reaction plate, with atmospheric insulation, it is preferably in solid contact therewith, conveniently by means of epoxy adhesive particularly when provided as resistive ribbons. The element could be arranged peripherally of the reaction plate. However, in order to provide a greater heating area than is available peripherally, it preferably traverses the plate. It is preferable for the bottom surface of the plate to be in continuous heat conducting contact with the

cooling means, which necessitates the elements extending internally of the plate. For this reason, the plate may be conveniently in two parts, with the heating element in grooves either in the bottom of the upper part or the top of the lower part - preferably the latter.

Alternatively, where heating element is a sheathed resistive wire, it may be accommodated in a serpentine groove in the bottom surface of the reaction plate. This grooved surface can be in direct contact with the Peltier effect devices.

With their side opposite from the reaction plate, the Peltier effect devices conveniently abut the heat sink. In the preferred embodiment, the heat sink is finned and an air circulator is provided for passing air over the fins and cooling them. Air may be circulated over the reaction plate as well, to contribute to its cooling. Alternatively it may be insulated.

In one embodiment, the machine includes means for switching the solid state heat pumps and the fans - when provided - OFF and the ohmic heating element ON during heating of the reaction plate, and the heat pumps and fans ON and the heating element OFF during cooling of the plate.

In another embodiment, the machine includes means for switching the solid state heat pump partially ON in their non-cooling sense, the fans - when provided - OFF and the ohmic heating element ON during heating of the plate, and the heat pump and fans ON and the heating element OFF during cooling of the plate. Conveniently this embodiment includes a mains-to-low-voltage transformer, a low-voltage rectifying circuit, and a series resistor. The switching means comprises a combined polarity-reversing and down-rating relay switch for applying in its normal state rectified low voltage of one polarity to the solid state heat pump during cooling and of the other polarity in its switched state to the heat pump with the series resistor connected in series during heating, a cooling

relay switch for applying low AC voltage from the transformer to the rectifying circuit for cooling (with the combined switch in its normal state) and a heating relay switch for applying low AC voltage from the transformer to the heating element for heating.

To help understanding of the invention, a specific embodiment thereof will now be described with reference to the accompanying drawings in which:-

The Drawings

Figure 1 is a perspective view of a biochemical machine according to the invention in combination with a micro processor for controlling the machine;

Figure 2 is a perspective view of the machine of Figure 1 with its case removed;

Figure 3 is an exploded view of the heat exchange components of the machine;

Figure 4 is an underneath plan view of the reaction plate of the machine;

Figure 5 is a circuit diagram of the machine;

Figure 6 is an exploded perspective view of another biochemical reaction machine according to the invention;

Figure 7 is a diagrammatic scrap side view of the lower part of a reaction plate of the machine of Figure 6;

Figure 8 is a diagrammatic scrap plan view of the part shown in Figure 7;

Figure 9 is a block diagram of control arrangements for the machine of Figure 6.

First Preferred Embodiment

Referring first to Figure 1, the biochemical reaction machine 1, also known as an incubator, is used in combination with a microprocessor 2. The latter is an independent unit which is normally positioned on top of the machine 1 and connected to it by a control cable. The hardware details of the microprocessor 2 are conventional and it will not be described further.

The machine 1 has a cover 3 for a reaction plate 4 shown in Figure 2. This figure shows the machine without its upper case 4. An aluminium reaction plate 5, accommodating a plurality of Eppendorf tubes 6 (or alternatively a microtitre plate or the like) in recesses 7 in its upper surface, is mounted over a finned, alumium heat sink 8. The reaction plate is 90 mm square by 10 mm deep. Front and rear cooling fans 9,10 are arranged to pass air through the fins 11 of the heat sink 8 for its cooling. Referring to Figure 3, the reaction plate 5 is urged firmly towards the heat exchanger by screws 12, sandwiching four aluminum spacer blocks between the reaction plate and the heat sink. To ensure good thermal contact silicon heat conduction compound is used at the sandwich joints. The upper surface, except at the recesses 7, and side edges of the reaction plate is covered in heat insulation foam plastics material, to obviate condensation during storage between 2°C and 8°C.

The lower surface of the reaction plate has a serpentine groove 14 in which is accommodated a sheathed resistance wire heating element 15. A temperature sensor 16 is accommodated in a bore 17 in one side edge of the reaction plate 5.

As shown in Figure 2, power and control circuitry is mounted in a compartment separated from the heat sink 8 and fans 9,10 by a panel 18. Thus, with the case fitted, these components are arranged in a self-contained air passage having front and rear openings in the case at the fans. Although some components of the power and control circuitry are shown in Figure 2, the irrelative physical position is arranged merely for convenience and not in accordance with their operational relationship which is shown in the circuit diagram of Figure 5.

The circuitry includes a fused power socket 20, on/off switch 21, neon power indicator 22 and a compartment cooling fan 23. The machine is powered via a mains to low voltage transformer 24 which has 24 volt and 9 volt tappings. The latter power an interface circuit 25, which is of conventional

design in converting control signals from the microprocessor to relay control currents. Three solid state relays 26,27,28 are under control of the interface 25, with a further mechanical relay 29 being under indirect control thereof via the relay 28. The relay 26 switches the heat-sink cooling fans 9,10 ON and OFF. They are powered by mains voltage. The Peltier devices 13, which are solid state heat pumps, are Melcor No. CPL 4-127-045L devices. The heating element 15 is a 200 watt heater. These components are powered at 24 volts from the transformer 25, the Peltier devices via a rectifier circuit 30.

The relay 27 switches 24 volts AC to the rectifier circuit and hence 24 volts DC to the Peltier devices which are connected to it by the relay 29. The relay 28 switches 24 volts AC to the heater 15 and the winding 31 of the relay 29. In its normal state, the relay 29 connects the four Peltier devices - which are series wired - to the rectifying circuit for passing 4 amps DC current to them for their operation in the cooling mode, that is pumping heat from the reaction plate to the heat sink. In its switched state, the relay switches a 10 ohm resistor 32 into series with the Peltier devices and reverses their polarity, whereby 2 amps in the non-cooling sense is passed to them. Since in use the reaction plate is normally hotter than the heat sink, this down-rating and reversal of the Peltier devices causes them to operate as insulators. (They conduct heat in their quiescent state). The sensor 16 is connected to the interface for passing out temperature information. All connections to the reaction plate, i.e. to the Peltier devices, heater element and sensor are via a plug and socket 31 to allow the plate and heat sink assembly to be changed as a service operation.

In use, the microprocessor, in accordance with a memorized temperature time programme which can involve temperatures from 4°C to 105°C and temperature change rates of 1°C/second, commands heating or cooling if the reaction plate is too cold or too hot as measured by the sensor 16. If cooling is

commanded, the relays 26 and 27 are switched to switch ON the fans 9,10 and Peltier devices 13. If heating is commanded, the relays 27 and 28 - and hence 29 - are switched to switch ON the heater 15, the rectifying circuit and the Peltier devices in reverse down-rated.

Second Embodiment

Referring to Figures 6 to 9 of the drawings, the second reaction machine has a two part, aluminium reaction plate 101 which has recesses 102 in its upper surface for reagent containing test tubes T, of which one is shown in Figure 4. In this embodiment, the plate 101 is 90 mm long by 90 mm wide and can accommodate 20 1.5ml tubes or more smaller tubes. The upper part 103 of the plate is 10mm deep and is bolted by non-shown bolts to a lower part 104 which is 3.5mm deep. This has a plurality of 4mm deep grooves 105 traversing its top surface. In each of these extends a resistive ribbon 106 set in epoxy resin 107. The ribbons are series connected at their ends by copper connectors 108, set in end blocks 109 of epoxy resin, to make up a 200 Watt heater. When the parts 103,104 are bolted together, the ribbon heater is fully incorporated in the reaction plate 101.

A semi-conductor temperature sensor 110 is set in the top surface of the plate 101, also with epoxy resin.

Four Peltier effect heat pump devices 111 are sandwiched between the plate 101 and a finned heat sink 112 in heat conducting contact with both. The combined capacity of the devices is approximately 100 Watts under the machine's working conditions.

At one axial end of the plate 101 and heat sink 112 is an air blowing fan 113 and at the other is an air sucking fan 114 which are arranged to pass air over the sink's fins 115 and the upper surface of the plate 101. For this the plate and sink are arranged with an openable casing which is not shown.

The machine includes a controller 116 which can be programmed to raise and lower the temperature of the reaction

plate 101 and the reagents in accordance with a predetermined temperature/time cycle. When the cycle requires an increase in temperature, the ribbon heater 106 is switched ON and the Peltier devices 11, together with the parallel connected fans 113,114, are switched OFF. When a decrease in temperature is required the heater is OFF and the devices 111 and fans 113,114 are ON. A typical temperature cycle passes from ambient to 37°C or 45°C to 70°C and back to ambient for appropriate times. The cycle may include repeated excursions to the same or different temperatures.

For accurate control of the reactions occurring, it is advantageous if the periods at steady temperature are separated by short periods of heating or cooling. The machines described are well adapted to this in that:-

1. During heating, the Peltier devices, even if not reversed as in first embodiment, in their passive condition conduct only moderately well since they comprise electrically insulating ceramic material sandwiching their semi-conductor active part. Hence the thermal mass to be quickly raised in temperature is restricted to the reaction plate together with the tubes and reagents. Typically with the plate described in prototype form a temperature rise from 40°C to 70°C was achieved in approximately 1.4 minutes.

2. At the elevated temperature of the plate , the heat sink will heat to a lower temperature, typically 55°C for a 70°C temperature of the reaction plate. This level of heating requires less wattage than if the heat sink required heating to 70°C. Further there is a time lag in the sink reaching its steady temperature as against the plate reaching its steady temperature. This lag enables the plate to be quickly heated and then restored to temperature by further heating as the Peltier devices slowly conduct heat to the sink for its heating.

3. When the cooling is required, a more moderature

temperature differential across the Peltier devices will have been established to cause them to operate more efficiently - than if for instance they had caused the block to be heated by pumping of heat from the sink.

4. The initial steady state sink tempeature of 55°C and the cooling air circulation keep the sink close in temperature to the reaction plate and hence the devices operating efficiently even after the temperature state has inverted to one when the heat sink is hotter than the reaction, plate.

5. In the second embodiment the air circulation over the top surface of the reaction plate augments the cooling rate of the Peltier heat pumps when active to provide a cooling rate as fast as the heating rate.

Claims

1. A biochemical rection machine comprising:-

a reaction plate for transferring heat to and from reagents accommodated by the reaction plate;

means for cooling the reaction plate, including a solid state heat pump in thermal contact on one side with the reaction plate and a heat sink in thermal contact with the other side of the solid state heat pump; and

means for heating the reaction plate;

wherein the heating means is adapted and arranged to transfer heat direct to the reaction plate substantially independently of heat transfer from the heat sink by the heat pump.

2. A biochemical reaction machine as claimed in claim 1, wherein the heating means is an ohmic heating element incorporated with the reaction plate.

3. A biochemical reaction machine as claimed in claim 2, wherein the ohmic heating element has a plurality of sections transversing the plate substantially from edge-to-edge.

4. A biochemical reaction machine as claimed in claim 3, wherein the sections of the element are arranged in a serpentine manner.

5. A biochemical reaction machine as claimed in claim 2, claim 3 or claim 4, wherein the ohmic heating element comprises a sheathed resistive wire received in groove(s) in the plate.

6. A biochemical reaction machine as claimed in claim 2, claim 3 or claim 4, wherein the ohmic heating element comprises resistive ribbons(s) received in groove(s) in the plate with the interposition of epoxy resin between the material of the plate and the ribbon(s).

7. A biochemical reaction machine as claimed in any one of claims 2 to 6, wherein the plate comprises an upper part and a lower part, the ohmic heating element being received between the parts.

8. A biochemical reaction machine as claimed in any preceding

claim, including means for removing heat from the heat sink.

9. A biochemical reaction machine as claimed in claim 8, wherein the heat removing means is at least one fan and the heat sink is finned for removal of heat from the heat sink by air moved by the fan(s).

10. A biochemical reaction machine as claimded in claim 9, wherein the fan(s) is(are) arranged to pass cooling air over a surface of the reaction opposite from the heat sink.

11. A biochemical reaction machine as claimed in any one of claims 1 to 9, wherein the reaction plate is insulated substantially over its entire surface except at its reagent accommodation positions and at the solid state heat pump.

12. A biochemical reaction machine as claimed in any one of claims 2 to 11, including means for switching the solid state heat pump and the fans - when provided - OFF and the ohmic heating element ON during heating of the reaction plate, and the heat pump and fans ON and the heating element OFF during cooling of the plate.

13. A biochemical reaction machine as claimed in any one of claims 2 to 11, including means for switching the solid state heat pump partially ON in their non-cooling sense, the fans - when provided - OFF and the ohmic heating element ON during heating of the plate, and the heat pump and fans ON and the heating element OFF during cooling of the plate.

14. A biochemical reaction machine as claimed in claim 13, including a mains-to-low-voltage transformer, a low-voltage rectifying circuit, and a series resistor; wherein the switching means comprises a combined polarity reversing and down-rating relay switch for applying in its normal state rectified low voltage of one polarity to the solid state heat pump during cooling and of the other polarity in its switched state to the heat pump with the series resistor connected in series during heating, a cooling relay switch for applying low AC voltage from the transformer to the rectifying circuit for cooling (with the combined switch in its normal state) and a

heating relay switch for applying low AC voltage from the transformer to the heating element for heating.

15. A biochemical reaction machine as claimed in claim 14, including a control circuit for switching the cooling relay switch ON for cooling, and the heating relay switch and the cooling relay switch ON for heating, the combined relay switch being connected to change to its switched state when the heating relay switch is ON.

16. A biochemical reaction machine as claimed in claim 15 wherein the control circuit is an interface for actuating the cooling relay switch in response to an external cooling control signal and the cooling and heating relay switches in response to an external heating control signal.

17. The combination of a biochemical reaction machine as claimed in claim 16, including a temperature sensor on the reaction plate, the interface being adapted to pass out a temperature indicative signal; and a microprocessor, having a memorized temperature/time programme, adapted to produce in response to the temperature indicative signal the cooling control signal if the reaction plate is hotter than the presently required temperature and the heating control signal if the reaction plate is cooler than the presently required temperature.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 8900684 SA 29509

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 13/10/89. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB-A- 2111301	29-06-83	DE-A- 3149624	23-06-83
		US-A- 4453385	12-06-84
DE-A- 3237406	05-05-83	JP-A- 58062564	14-04-83
		JP-A- 58062565	14-04-83
		JP-A- 58062566	14-04-83
		US-A- 4548259	22-10-85
DE-B- 1077460		None	
DE-A- 3441179	22-05-86	None	

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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FIG. 1

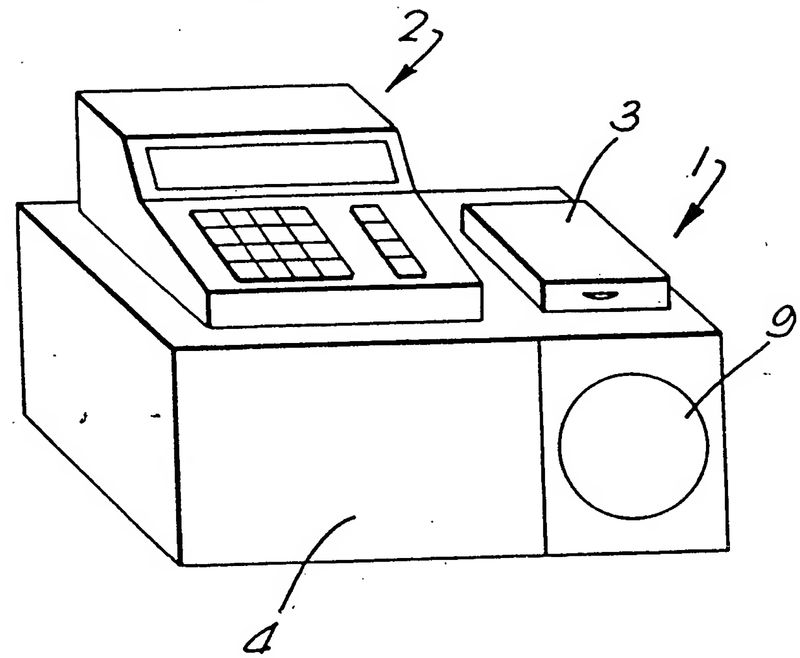


FIG. 2

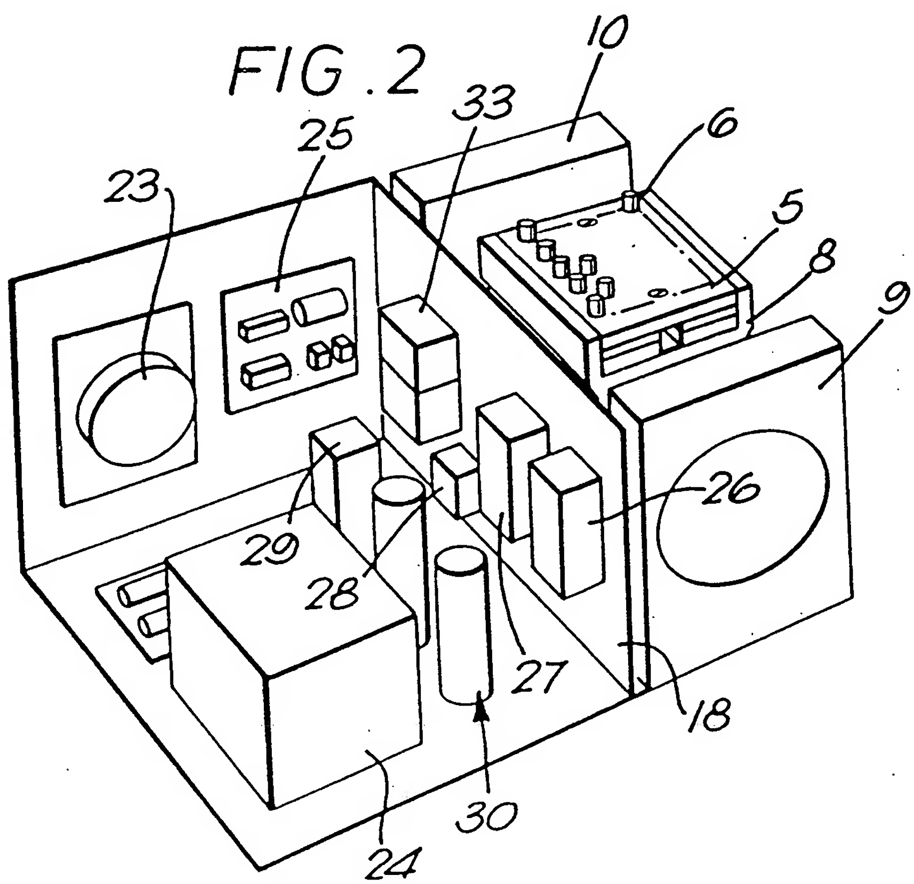


FIG. 3

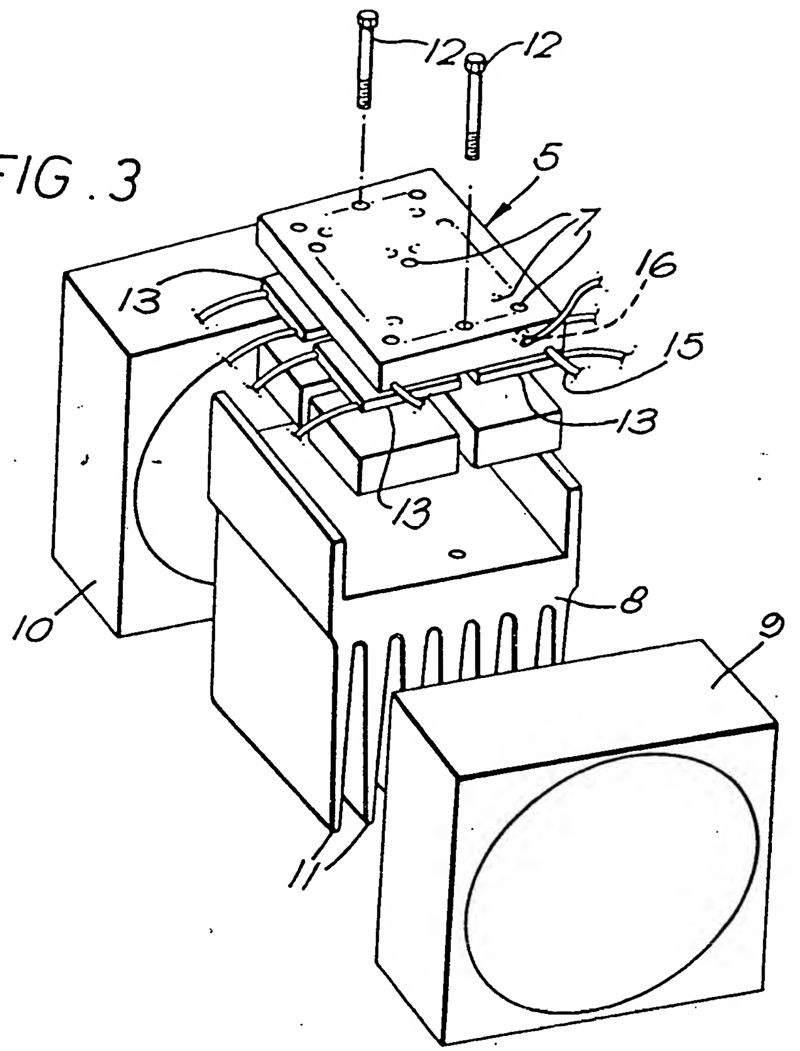


FIG. 4

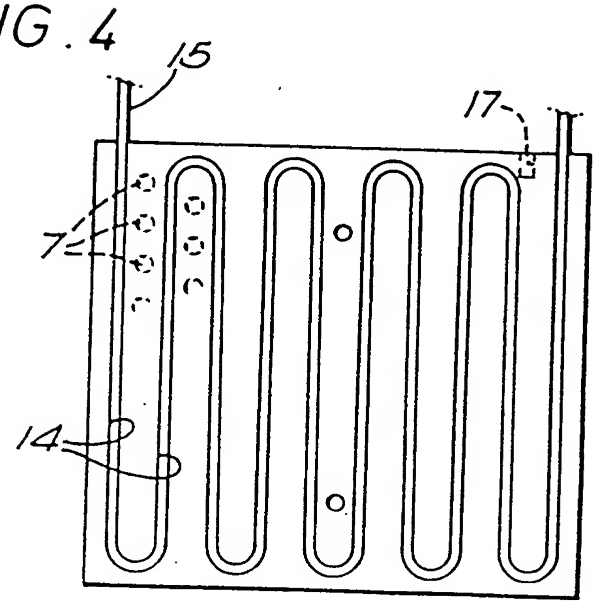
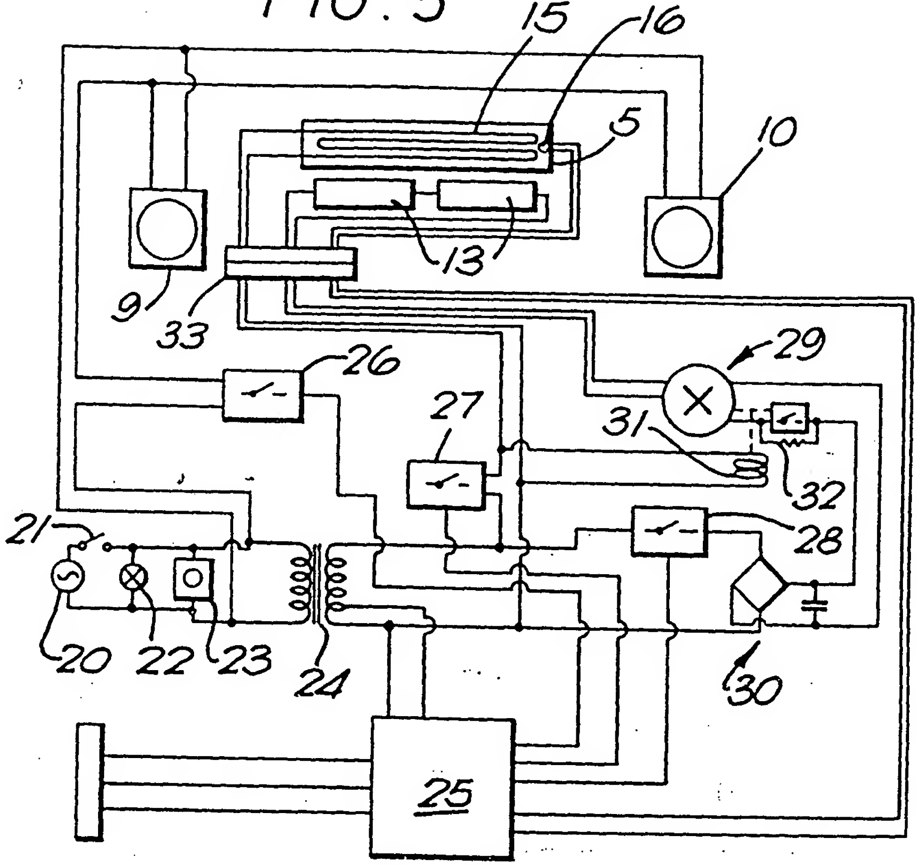


FIG. 5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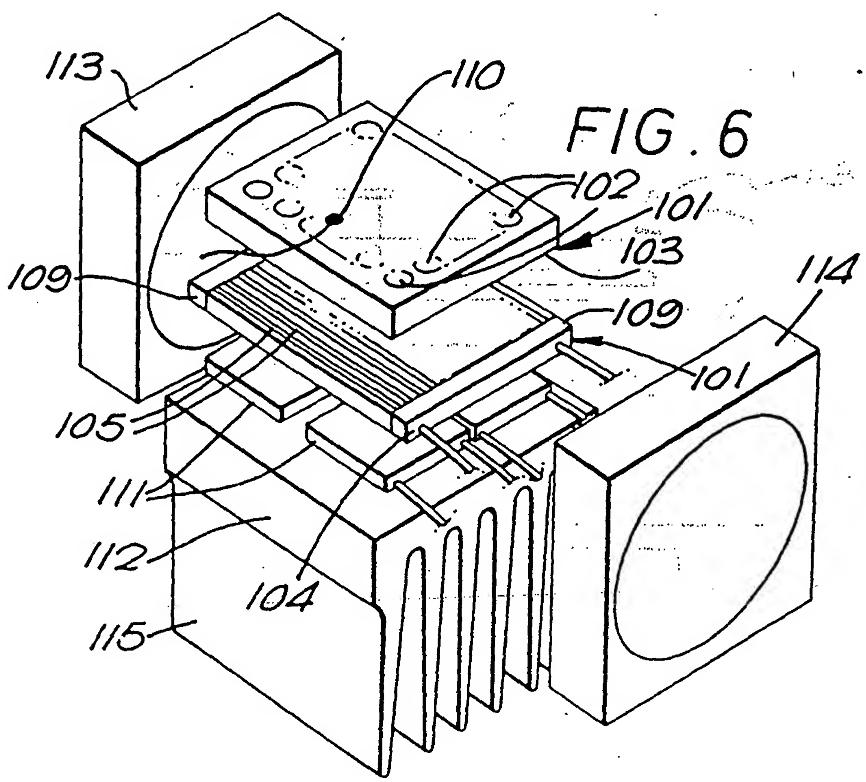
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FIG. 6